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athematical Biophysics

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BULLETIN OF
MATHEMATICAL BIOPHYSICS
VOLUME 2, 1940

THE EQUIVALENCE OF THE CONDUCTION THEORIES OF RASHEVSKY AND RUSHTON

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The one-factor, semi-formal nerve conduction theory of Rashevsky and the dynamical theory of Rushton are shown to be completely equivalent.

In 1933 N. Rashevsky proposed a semi-formal theory of nerve conduction based on the excitation theory of H. A. Blair (1932) and on the theory of local re-excitation by action currents. This theory is "semi-formal" in the sense that in it the excitation process is considered purely *formally,* while the distribution of currents in nerve is calculated on the *dynamical* assumption that a nerve fiber is a pure resistance network (Figure 1 a).

Four years later, W. A. H. Rushton (1937) proposed a dynamical theory of excitation and conduction in which a nerve fiber is considered to be a resistance-capacitance network (Figure 1 b) and excitation occurs when θ, the charge (or voltage) across the nerve membrane (or capacitance in the network), exceeds a certain critical value, θ_c. Excitation in both theories is characterized by the appearance of an action E.M.F. in series with the nerve sheath (Figures 1 c, 1 d) at the excited point.

We shall now show that the two theories are formally equivalent and that Rushton's model may be considered as a dynamical instance of Rashevsky's semi-formal theory.

The fundamental equation of Rushton's theory describes the variation of charge, θ, along a line consisting of an unexcited portion (Figure 1 b) joined to an excited portion (Figure 1 d). This equation is given by Rushton (1937) as

$$\left(\frac{\partial^2}{\partial x^2} - \frac{1}{L^2}\right)\left(\frac{\partial \theta}{\partial t} + \frac{\theta}{\alpha}\right) = -\frac{r_1}{R}\frac{\partial I}{\partial x} - \frac{\partial^2 E_x}{R \partial x^2} \qquad (1)$$

where

r_1 = resistance per unit length of interstitial fluid.
r_2 = resistance per unit length of axis cylinder.
$\frac{1}{R}$ = conductance per unit length of sheath for radial currents.

$\frac{1}{\rho}$ = conductance per unit length of membrane. $(\frac{1}{\rho} >> \frac{1}{R})$.
θ = charge per unit length of membrane.
c = capacitance of membrane per unit length.
$L^2 = R/(r_1 + r_2)$.
$\alpha = c\rho$
$I = i_1 + i_2$ = sum of currents flowing parallel to nerve outside and inside. ($I = 0$ except between stimulating electrodes.)
$E_x = 0$ in resting region.
$= E$ in excited region.

The derivation of Rashevsky's fundamental equation requires two steps. First, an elementary application of Kirchhoff's laws to a line consisting of unexcited and excited portions (Figures 1a and 1c) joined at the point of excitation gives for the space variation of the current, i, flowing through the myelin sheath, R,

$$\left(\frac{\partial^2}{\partial x^2} - \frac{1}{L^2}\right) i = -\frac{r_1}{R}\frac{\partial I}{\partial x} - \frac{1}{R}\frac{\partial^2 E_x}{\partial x^2} \,, \tag{2}$$

where the constants have the same meaning as before. Second, the time variation of the formal excitatory state, p, is given by Blair's equation

$$\frac{\partial p}{\partial t} = Ki - kp \,, \tag{3}$$

where K and k are constants, and excitation occurs when p exceeds a critical value p_c. Elimination of i between equations (2) and (3) gives

$$\frac{1}{K}\left(\frac{\partial^2}{\partial x^2} - \frac{1}{L^2}\right)\left(\frac{\partial p}{\partial t} + kp\right) = -\frac{r_1}{R}\frac{\partial I}{\partial x} - \frac{\partial^2 E_x}{R\partial x^2} \,. \tag{4}$$

Equation (4) is identical with (1) if p/K is identified with the membrane charge θ, and $1/k$ is put equal to α, the relaxation time of the membrane condenser.

Since all the results of Rushton's theory follow directly from equation (1), and since Rashevsky's theory leads to a formally identical equation, it may be concluded that the two theories are identical. For example, the original expression for the velocity of the impulse was given by Rashevsky as

$$v = L\,\lambda\,k \tag{5}$$

where λ, the safety factor, is defined by

$$\lambda = \frac{\text{action current} - \text{rheobasic current}}{\text{rheobasic current}};$$

or, since current and voltage are proportional,

$$\lambda = \frac{\text{action voltage} - \text{rheobasic voltage}}{\text{rheobasic voltage}}.$$

Rushton's velocity formula is

$$v = \frac{L\lambda}{\alpha}, \tag{6}$$

which of course is identical with (5) if $k = 1/\alpha$.

Whether Rushton's resistance-capacitance model is the only purely electrical model which is equivalent to Rashevsky's semi-formal model cannot be ascertained a priori. The development of other dynamical models which are equivalent to these two may be of interest because they would allow for a greater flexibility in the interpretation of conduction phenomena.

This work was aided by a grant from the Dr. Wallace C. and Clara A. Abbot Memorial Fund of the University of Chicago.

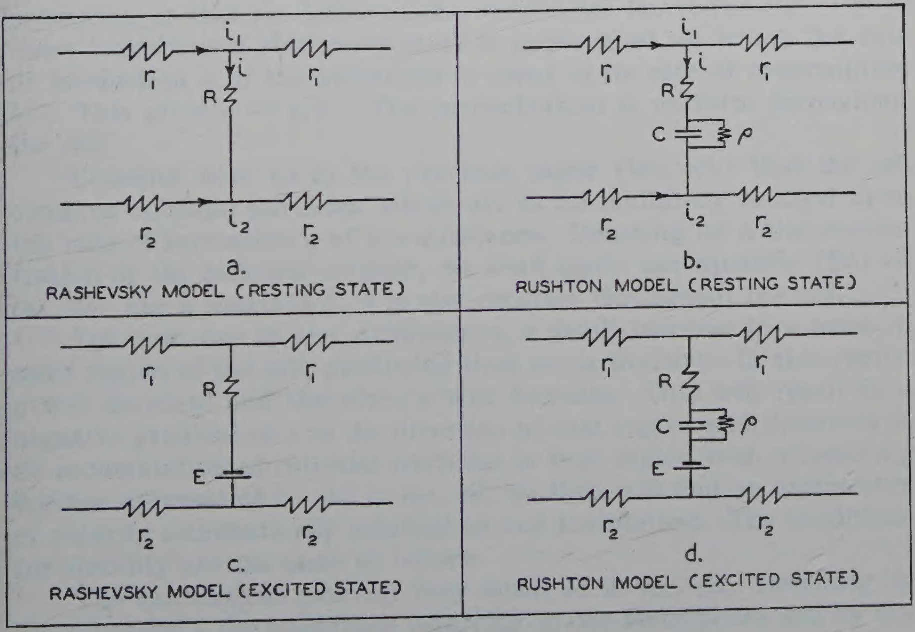

FIGURE 1

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BULLETIN OF
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FURTHER CONTRIBUTIONS TO THE THEORY OF CELL POLARITY AND SELF-REGULATION

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In continuation of a previous study a case of self-regulating polarity is investigated, in which a metabolite neither enters nor leaves the cell, being produced in one part of it and consumed in another. Such a cell possesses a larger degree of autonomy and independence of external conditions than the previously discussed one. Application to cellular locomotion is indicated.

This study is a continuation of a previous paper (Rashevsky, 1940; hereinafter referred to as *loc. cit.*).

Consider a spherical cell of radius r_0, inside of which a substance is produced at a rate of q gm cm^{-3} sec^{-1}. Let the same substance break down and therefore disappear at a rate proportional to its concentration c, and given by $-bc$ gm cm^{-3} sec^{-1}.

Let the membrane of the cell be completely impermeable to that substance, so that the latter neither enters nor leaves the cell. Under these conditions a stationary state is approached, in which the rate of production q of the substance is equal to its rate of consumption bc. This gives $c = q/b$. The concentration is uniform throughout the cell.

Consider now, as in the previous paper (*loc. cit.*) that the cell contains colloidal particles, which act as an inhibitory catalyst upon the rate of formation q of the substance. Denoting by n the concentration of the colloidal catalyst, we shall again use equation (24) of *loc. cit.* For a constant c, n is also constant throughout the cell.

Let now, due to any disturbance, a small increase in n arise in some region of the cell, producing thus an asymmetry. In this region q will decrease and therefore c will decrease. This will result in a negative gradient of c in the direction of that region and therefore in an accumulation of colloidal particles in that region with a resulting further decrease of c. As in *loc. cit.* we thus will find an asymmetry or polarity automatically established and maintained. The conditions for stability are the same as before.

The calculations proceed very much as in *loc. cit.* Denoting by the subscript 1 the quantities referring to one hemisphere and by the subscript 2 those referring to the other hemisphere and remembering that in the stationary state the total amounts produced in one hemisphere equal the total amount consumed, plus the total amount diffusing into the other hemisphere, we have

$$\begin{aligned} &\tfrac{2}{3}\pi r_0{}^3 q_1 - \tfrac{2}{3}\pi r_0{}^3 b c_1 - \pi r_0 D (c_1 - c_2) = 0\,, \\ &\tfrac{2}{3}\pi r_0{}^3 q_2 - \tfrac{2}{3}\pi r_0{}^3 b c_2 + \pi r_0 D (c_1 - c_2) = 0\,. \end{aligned} \tag{1}$$

Solving for c_1 and c_2 and calculating the quantity $c_1 - c_2$, we find:

$$c_1 - c_2 = \frac{r_0{}^2}{r_0{}^2 b + 3D}\,(q_1 - q_2)\,. \tag{2}$$

For the relation between the quantity $x = c_1 - c_2$ and $n_2 - n_1$ we have equation (23) of *loc. cit.* In its dependence on $q_1 - q_2$ equation (2) is similar to equation (18) of *loc. cit.* Hence, putting

$$\frac{r_0{}^2}{r_0{}^2 b + 3D} = A \tag{3}$$

we shall have for $x = c_1 - c_2$ formally the same expressions as those obtained previously.

In view of the assumed impermeability of the cell membrane to the substance in question, such a cell possesses an autonomy and independence of external conditions to a much greater degree than before.

An interesting consequence may be considered here. Let the membrane, while impermeable to the metabolite, be freely permeable to water. The osmotic pressure due to the concentration of the metabolite and directed outward, will be greater at the pole, at which the concentration is greater. Therefore a net resultant force in the direction of that pole will be present, and the cell in that case will move forward with the pole of higher concentration. At first sight this conclusion sounds like a paradox, for we seem to have a movement due to internal forces. This however is not so, since inside the cell the substance flowing from one pole to another exerts a diffusion drag (Young, 1939) upon the water, which even inside the cell remains stationary, due to the assumed complete permeability of the cell membrane to water.

Somewhat similar cases of spontaneous locomotion have been studied by Gale Young (unpublished) for the case of an asymmetric flow of a substance from the cell. In that case the mechanism of locomotion is much like that of a rocket. In the present case the mechanism may be to some extent compared with a sort of caterpillar drive. Such mechanisms may well be responsible in some cases for spontaneous locomotion of unicellular organisms.

The author is indebted to Mr. H. D. Landahl for checking the algebra.

This work has been aided in part by a grant from Dr. Wallace C. and Clara A. Abbot Memorial Fund of the University of Chicago.

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CONTRIBUTIONS TO THE MATHEMATICAL THEORY OF ORGANIC FORM. II

ASYMMETRIC METABOLISM OF CELLULAR AGGREGATES

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The case is studied of a cellular aggregate forming a hollow spherical shell, the physical constants and the metabolic rate being non-uniform throughout the shell. This leads to asymmetries of concentration distributions, which are calculated here for some simple cases.

In a previous paper (Rashevsky, 1940 b) we have investigated the mechanism of formation of a hollow shell from a densely packed cellular aggregate. This has been done especially with a view of possible applications to the formation of a blastula.

When, as is actually the case, the original cell from which all the cells of the blastula descend, is not uniform in its physico chemical constitution, then the cellular shell, forming the blastula, will also be nonuniform. This nonuniformity may manifest itself in a variation of the diffusion coefficients and permeabilities along the surface of the shell or in similar variations of the rates of reactions or both. For reference in future studies, we shall derive here some formulae for such a nonuniform shell. For simplicity we shall consider here the case of an infinite surface permeability and of an infinite external diffusion coefficient for one substance, produced or consumed by cells of the shell.

Let the approximately spherical shell have an internal radius, r_0, a thickness $\delta < < r_0$ and be characterized by the following nonuniformity. Within a single-connected region 1, occupying a fraction α of the surface of the shell, the diffusion coefficient will be assumed to be D_1, the rate of reaction q_1. In the remaining part of the shell, 2, the diffusion coefficient has the value D_2, the rate of reaction — the value q_2. The external concentration of the metabolized substance is denoted by c_0. Due to the infinite permeability, c_0 is also the inside concentration of the substance at the outer surface of the shell.

If the shell were uniform in all respects, then the concentration inside the shell at the inner surface would also be the same at all points of the surface and within the cavity. Due to the nonuniformities assumed above, we shall have in general different concentrations c_1 and c_2 in the two regions. Again, due to the assumption of infinite permeability, c_1 and c_2 represent also the concentrations of the substance inside the cavity in the immediate neighborhood of the shell.

Due to this nonuniformity of concentration inside of the cavity, there will be not only a transport of the substance between the shell and the external medium, but there will also be a flow of substance inside the cavity. This flow will be determined by the average gradient and the cross-section through which the flow takes place. The average gradient in the direction from 2 to 1 is of the order of magnitude of $(c_1 - c_2)/d$ where d is the average distance over which c varies from c_1 to c_2. Therefore, denoting by D_0 the diffusion coefficient of the liquid in the cavity, the flow per cm² per second is of the order of $D_0(c_1 - c_2)/d$. The assumption of a finite D_0 and infinite external diffusion coefficient D_e is not a self-contradicting one, for the cavity may contain solutes, for which the cells of the shell are impermeable and which are practically absent in the outside. In any case the assumption $D_e = \infty$ does not introduce any fundamental restrictions. The total flow within the cavity from region 1 to 2 is equal to $D_0(c_1 - c_2)S/d$, where S is the average cross-section, through which the flow takes place.

From physical considerations it is apparent that when α is very small, then practically everywhere inside the cavity the concentrations c will be equal to c_2, and only in a very small region will c be equal to c_1. Therefore the average gradient will extend only over a very small region. Thus with α tending to zero, d also tends to zero. It also tends to zero as α tends to 1. For $\alpha = \frac{1}{2}$, when just half the shell has one set of constants, and half another one, d has a maximum and is of the order of magnitude of r_0. Approximately we may therefore put

$$d = 4r_0\,\alpha(1 - \alpha)\,, \tag{1}$$

which is one of the simplest expressions having the required property.

Similarly the average cross-sectional area S is zero for $\alpha = 0$ and $\alpha = 1$, and is of the order of πr_0^2 for $\alpha = \frac{1}{2}$. We put

$$S = 4\pi r_0^2\,\alpha(1 - \alpha)\,. \tag{2}$$

With these approximations the flow within the cavity is equal to

$$\pi r_0 D_0(c_1 - c_2)\,. \tag{3}$$

The concentrations c_1 and c_2 are determined in the usual way by considerations of material balance (Rashevsky, 1940 a, chapter i). The amount of substance metabolized in the region 1 equals $4\pi r_0^2 \alpha \delta q_1$. It is also equal to the difference between the amount $4\pi r_0^2 \alpha D_1 (c_1 - c_0)/\delta$ flowing outward and the amount given by (3), coming to the region 1 from within the cavity:

$$4\pi r_0^2 \alpha D_1 \frac{c_1 - c_0}{\delta} + \pi r_0 D_0 (c_1 - c_2) = 4\pi r_0^2 \alpha \delta q_1 . \tag{4}$$

Similarly, for region 2:

$$4\pi r_0^2 (1-\alpha) D_2 \frac{c_2 - c_0}{\delta} - \pi r_0 D_0 (c_1 - c_2) = 4\pi r_0^2 (1-\alpha) \delta q_2 . \tag{5}$$

The second term, on the left hand sides of equations (4) and (5) have opposite signs, because when inside the cavity the substance is transported *towards* region 1, it is transported *away* from region 2, and *vice versa.*

Introducing the notations

$$D = \alpha \bar{D}_1 + (1-\alpha) D_2 ; \quad \bar{q} = \alpha q_1 + (1-\alpha) q_2 , \tag{6}$$

we obtain from equations (4) and (5) after some rearrangements

$$c_1 = c_0 + \frac{4\alpha(1-\alpha) D_2 \delta^2 r_0 q_1 + D_0 \delta^3 \bar{q}}{4\alpha(1-\alpha) r_0 D_1 D_2 + D_0 \bar{D} \delta} \tag{7}$$

and

$$c_2 = c_0 + \frac{4\alpha(1-\alpha) D_1 \delta^2 r_0 q_2 + D_0 \delta^3 \bar{q}}{4\alpha(1-\alpha) r_0 D_1 D_2 + D_0 \bar{D} \delta} \tag{8}$$

For $D_1 = D_2 = \bar{D}$; $q_1 = q_2 = \bar{q}$ equations (7) and (8) reduce to

$$c_1 = c_2 = c_0 + \frac{\delta^2 \bar{q}}{\bar{D}} , \tag{9}$$

an expression that can be obtained directly. For not too small values of α and for $D_0 \infty D_1 \infty D_2$ equations (7) and (8) reduce to

$$c_1 = c_0 + \frac{\delta^2 q_1}{D_1} ; \quad c_2 = c_0 + \frac{\delta^2 q_2}{D_2} . \tag{10}$$

The author is indebted to Mr. H. D. Landahl for checking the algebra, and for valuable suggestions and comments.

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A CONTRIBUTION TO THE MATHEMATICAL BIOPHYSICS OF PSYCHOPHYSICAL DISCRIMINATION III

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The neural mechanism previously discussed is further generalized. The case is considered in which a random variation is associated with each stimulus. The mechanism is generalized and equations are derived for discriminations between stimuli differing in several modalities. The latter indicates an analysis by the factor method. Suggestions are made in connection with the use of triads and with the problem of a multidimensional psychophysics.

It is the purpose here to generalize, in two different directions, the neural mechanism previously described (Landahl, 1938, 1939; hereinafter referred to as A and B respectively). Reference shall be made to the diagramatic representation of the mechanism of Figure 1 of the first paper (A) by writing Figure 1 (A). The notation used here shall conform to that previously used and is largely the same as the notation used by N. Rashevsky (1938).

I. One modality but with independent fluctuations. In the previous discussions it was considered that a random fluctuation occurred only at one synapse since the results would be essentially unchanged by introducing independent fluctuations at both s_1 and s_2 of Figure 1(A). We proceed to show that this is so, then to investigate some conditions under which the more general consideration would lead to predictions necessarily absent from the simpler case.

Let $p_1(\varepsilon - j)'_1 d(\varepsilon - j)'_1$ be the probability that the random fluctuation at s_1 has a value which lies between $(\varepsilon - j)'_1$ and $(\varepsilon - j)'_1 + d(\varepsilon - j)'_1$ so that if

$$\alpha_1 = \frac{(\varepsilon - j)'_1}{\sqrt{2}\,\sigma_1}\,, \tag{1}$$

then, assuming a Gaussian distribution,

$$p_1 = \frac{1}{\sqrt{2\pi}\,\sigma_1} e^{-\alpha_1^2}\,, \tag{2}$$

where σ_1 is the standard deviation of the distribution function at s_1. Similarly if

$$\alpha_2 = \frac{(\varepsilon - j)'_2}{\sqrt{2}\,\sigma_2}\,, \tag{3}$$

$$p_2 = \frac{1}{\sqrt{2\pi}\,\sigma_2}\, e^{-\alpha^2_2}\,, \tag{4}$$

where σ_2 is the standard deviation of the distribution function at s_2 and p_2 is the ordinate of the same function.

After the stimuli S_1 and S_2 have been simultaneously presented (Landahl, 1940), there develops at s_1 and s_2 the excitation factors ε_1 and ε_2 respectively. These are functions of S_1 and S_2 respectively, and both are functions of time. Considering only the stationary state, so that, as $t >> 1/a$ in equations (4) of the former development (A), the latter may be written, because of equations (1) of (A),

$$\varepsilon_1 = \frac{AK}{a} \log \frac{S_1}{h_0} \tag{5}$$

$$\varepsilon_2 = \frac{AK}{a} \log \frac{S_2}{h_0}\,. \tag{6}$$

Superimposed on the amounts ε_1 and ε_2 at s_1 and s_2 respectively [Figure 1 (A)] are the random changes $(\varepsilon - j)'_1$ and $(\varepsilon - j)'_2$. The total amount at s_1 is then $\varepsilon_1 + (\varepsilon - j)'_1$, and that at s_2 is $\varepsilon_2 + (\varepsilon - j)'_2$. In order that S_1 produce its corresponding response, which we shall call "correct", it is necessary and sufficient that the difference between the total amount of the excitation factor at s_1 and the total amount at s_2 be greater than some quantity h (A, pp. 111, 115, and B, p. 165). Then the threshold, h', of fiber III of Figure 1 (A) is exceeded and a "correct" response produced. For a correct response we have

$$\varepsilon_1 + (\varepsilon - j)'_1 - \varepsilon_2 - (\varepsilon - j)'_2 > h\,. \tag{7}$$

Similarly for a wrong response we have

$$\varepsilon_1 + (\varepsilon - j)'_1 - \varepsilon_2 - (\varepsilon - j)'_2 < -h\,; \tag{8}$$

and for no response, which we shall identify with an "equality" (doubtful) response, we have

$$h \geqslant \varepsilon_1 + (\varepsilon - j)'_1 - \varepsilon_2 - (\varepsilon - j)'_2 \geqslant -h\,. \tag{9}$$

Now the probability, f, that $(\varepsilon - j)'_1$ and $(\varepsilon - j)'_2$ each have specified values is given by $f = p_1\, p_2$ if the events are uncorrelated, but if not, then, designating the correlation coefficient by r, we have

$$f = \frac{1}{2\pi\sigma_1\sigma_2\sqrt{1-r^2}} e^{-\frac{(a^2_1 - 2r\ a_1 a_2 + a^2_2)}{(1-r^2)}} . \tag{10}$$

Inequality (7) may be written

$$(\varepsilon - j)'_1 - (\varepsilon - j)'_2 > h - \varepsilon_1 + \varepsilon_2 , \tag{11}$$

or defining

$$(\varepsilon - j)' = \sqrt{2}\,\sigma\,\alpha = (\varepsilon - j)'_1 - (\varepsilon - j)'_2 , \tag{12}$$

so that

$$\sigma\,\alpha = \sigma_1\,\alpha_1 - \sigma_2\,\alpha_2 , \tag{13}$$

(11) may be written

$$(\varepsilon - j)' > -(\varepsilon_1 - \varepsilon_2 - h) . \tag{14}$$

The probability, $p(\varepsilon - j)'$ that $(\varepsilon - j)'$ has a particular value is given by replacing $\sqrt{2}\,\sigma_2\,\alpha_2$ by $\sqrt{2}\,\sigma_1\,\alpha_1 - \sqrt{2}\,\sigma\,\alpha$ in equation (10) and integrating the resulting function of α_1, $f(\alpha_1)$, with respect to $\sqrt{2}\,\sigma_1\,\alpha_1$ over all possible values of α_1, that is, from $-\infty$ to $+\infty$. Therefore, introducing (13) or its equivalent, $\alpha_2 = (\sigma_1\alpha_1 - \sigma\alpha)/\sigma_2$, into (10), and rewriting the exponent as a perfect square and a constant term, we obtain, on integrating.

$$p(\sqrt{2}\,\sigma\,\alpha) = \frac{e^{-\sigma^2 a^2/(\sigma^2_1 - 2r\sigma_1\sigma_2 + \sigma^2_2)}}{2\pi\sigma_1\sigma_2\sqrt{1-r^2}} \times$$

$$\int_{-\infty}^{+\infty} e^{-\frac{1}{1-r^2}\left[\frac{a_1}{\sigma_1}\sqrt{\sigma^2_1 - 2r\sigma_1\sigma_2 + \sigma^2_2} - \frac{\sigma\sigma_1 - r\sigma_1\sigma_2}{\sqrt{\sigma^2_1 - 2r\sigma_1\sigma_2 + \sigma^2_2}}\right]} d(\sqrt{2}\,\sigma_1\,\alpha_1) \tag{15}$$

$$= \frac{e^{-\sigma^2 a^2/(\sigma^2_1 - 2r\sigma_1\sigma_2 + \sigma^2_2)}}{\sqrt{2\pi(\sigma^2_1 - 2r\,\sigma_1\,\sigma_2 + \sigma^2_2)}} ,$$

or because of (12)

$$p(\varepsilon - j)' = \frac{1}{\sqrt{2\pi}\sqrt{\sigma^2_1 - 2r\,\sigma_1\,\sigma_2 + \sigma^2_2}} e^{-\frac{(\varepsilon - j)'^2}{2(\sigma^2_1 - 2r\sigma_1\sigma_2 + \sigma^2_2)}} . \tag{16}$$

Equation (16) is the equation of a Gaussian curve whose standard deviation is the square root of the expression in parentheses in the denominator of the exponent. We may for convenience define that value as σ without violating the previous definition of σ of equation (12), introduced to make the equations symmetric; or

$$\sigma = \sqrt{\sigma^2_1 - 2r\,\sigma_1\,\sigma_2 + \sigma^2_2} \tag{17}$$

and equation (15) may also be written

$$p = \frac{1}{\sqrt{2\pi}\,\sigma} e^{-a^2} . \tag{18}$$

The probability of a correct response, P_c, is given by integrating $p(\varepsilon - j)'$ over all values which satisfy the condition for a correct response given by (14) which is the same as (7). Then integrating $p(\varepsilon - j)'$ with respect to $(\varepsilon - j)'$ from $-(\varepsilon_1 - \varepsilon_2 - h)$ to ∞, we obtain

$$P_c = \int_{-(\varepsilon_1-\varepsilon_2-h)}^{\infty} p(\varepsilon - j)'\, d(\varepsilon - j)' . \tag{19}$$

Similar expressions may be written for the probability of a wrong response, P_w, and the probability of an equality response P_d. Although each stimulus has a separate fluctuation associated with it, the mechanism predicts that only a resultant fluctuation will be observed, and it will be a function of the situation as a whole.

Hence, if there are two independent or partially independent fluctuations instead of one, we obtain the same equations where a particular average of the two fluctuations, given by (17), is used. We have considered the separate variations as occurring at s_1 and s_2 of Figure 1 (A). Instead we may consider the random fluctuation as occurring at any point along the line of fibers traveled by the two respective groups of impulses (represented in the figure by fibers I and II).

Consider the following case. Let the mechanism by symmetric so that we have $\sigma_1 = \sigma_2$ and hence

$$\sigma = \sigma_1 \sqrt{1 - r} . \tag{20}$$

Let a group of stimuli $S_1, S_2 \cdots$ be presented in pairs so that from the distribution of judgments we may obtain the standard deviation in terms of some function of the external stimulus, in particular, in terms of the logarithm of the stimulus (or what is equivalent, since $S_1 \backsim S_2$, in terms of the per cent change in the stimulus). The value σ is measured in units of ε. If $k = a/AK$, we obtain $k\sigma = k\sigma'$, a particular value of the standard deviation in terms of the per cent change in the stimulus. Now let the external conditions be changed such that we may assume that the parameters of the mechanism of Figure 1 (A) are unchanged but that σ_1 and hence σ of (20) may have changed. We shall also assume that r of (20) is unchanged. Then let the same set of stimuli be presented in the same manner as before so that we may obtain $k\sigma = k\sigma''$, another experimental value.

Now let the stimuli be again presented in the same manner except that always one of the pair is under the condition for obtaining $k\,\sigma'$ and the other is under the condition for obtaining $k\,\sigma''$. We then obtain a value $k\bar{\sigma}$. If the only change can be attributed to the changes in σ, then $\bar{\sigma}$ will be given by an expression of the same form as the right member of equation (17) with, however, σ_1 replaced by $\sigma'_1 = \sigma'/\sqrt{1-r}$ and σ_2 replaced by $\sigma''_1 = \sigma''/\sqrt{1-r}$ [equation (20)], or

$$\bar{\sigma} = \frac{1}{\sqrt{1-r}}\sqrt{\sigma'^2 - 2\,r\,\sigma'\,\sigma'' + \sigma''^2}\,, \tag{21}$$

and hence

$$k\bar{\sigma} = \frac{1}{\sqrt{1-r}}\sqrt{(k\sigma')^2 - 2r(k\sigma')(k\sigma'') + (k\sigma'')^2}\,. \tag{22}$$

The terms on the right of equation (22) are experimentally given except for r. Since $k\bar{\sigma}$ is an empirical value, r may be evaluated for any one set of values $k\bar{\sigma}$, $k\sigma'$ and $k\sigma''$. Choosing different experimental conditions, a new set of values $k\bar{\sigma}$, $k\sigma'$ and $k\sigma''$ will be obtained and r may again be computed and so compared with the previous value of r. However, it must be remembered that besides assuming r to be constant throughout, we assume that AK/a and h_0 of equations (5) and (6) are unchanged. Should one of the assumptions not be tenable, we may change our purpose and use the same data to attempt measurement of the variation of one of the parameters.

It was previously pointed out (B., p. 163) that, on the basis of the mechanism of Figure 1 (A) and on the assumptions made, a scale value was proportional to $\varepsilon_1(S_1) - \varepsilon_2(S_2)$, both being proportional to the abscissa deviate corresponding to the ordinate of the cumulative frequency curve equal to the proportion of judgments $S_1 > S_2$. Now σ_1 and σ_2 of equation (17) are measures of the degree of fluctuation associated with the stimuli S_1 and S_2 respectively; σ measures the degree of the resultant fluctuation associated with the stimuli as they are compared, and is a measure of the distribution of the judgments of the pair. Equation (17) then gives the resultant fluctuation for a pair of stimuli in terms of that of each stimulus. If we measure $\varepsilon_1(S_1) - \varepsilon_2(S_2)$ in terms of the standard deviation of the resultant distribution we may write

$$\varepsilon_1(S_1) - \varepsilon_2(S_2) = X_{12}\,\sigma_{12}\,, \tag{23}$$

but because of (17)

$$\varepsilon_1(S_1) - \varepsilon_2(S_2) = X_{12}\sqrt{\sigma^2_1 - 2\,r\,\sigma_1\,\sigma_2 + \sigma^2_2} \tag{24}$$

where X_{12} is the deviate (Guilford, 1936, ch. VII) obtained when S_1 and S_2 are compared and $\sigma_{12} = \sigma$, the indices being introduced for definiteness.

That equation (24) is similar to the equation of the Law of Comparative Judgment (Thurstone, 1927) is not accidental. (Notice differences in the notation.) Statistically the problem here is essentially the same. The similarity is due to the assumption that the left terms are algebraically additive as well as to the assumption of normality. It is a fundamental assumption in N. Rashevsky's development (Rashevsky, 1938) that the excitation factor, as well as the inhibition factor, is subject to algebraic addition.

In equation (24) none of the terms except X_{12} is directly measurable. However, if both sides of equation (24) are multiplied by k as in (22), the left hand side becomes the per cent difference in the external stimulus magnitudes and on the right is the product of the deviate value X_{12} and the standard deviation in terms of the per cent change of stimulus value. All terms are then experimentally measurable. The equation only implies that the distribution of correct or wrong judgments if plotted in terms of a per cent change in stimulus, or even better, in terms of the logarithm of the stimulus, will be accurately represented by the integral of a Gaussian distribution curve (Guilford, 1936, p. 100). If such is not the case to a degree of accuracy demanded by experiment, then the assumption implied in equations (5) and (6) [equations (1) A] is not sufficiently accurate so that it is necessary to leave unspecified the $\varepsilon(S)$ relation (B, p. 163).

Summary. It has been shown that the previous assumption (A, B) of a random fluctuation confined to one synapse instead of two was justified. Except in unusual situations the substitution for σ from equation (17) generalizes the previous results to include a randomness associated with both stimuli. An experimental procedure is suggested in which it may be possible to obtain evidence for some of the assumptions made or to measure the variation of some external parameter with external conditions.

II. Discrimination of stimuli having differences in more than one modality. Thus far we have always assumed that the stimuli to be compared differ in but one modality. Let us consider the case in which the stimuli differ in more than one respect. Let the two stimuli S and $\bar{S}$, the latter being the standard, have the components S_1, S_2 $\cdots S_k$, $\cdots S_p$ and $\bar{S}_1$, $\bar{S}_2 \cdots \bar{S}_k$, $\cdots \bar{S}_p$ in the modalities 1, 2, $\cdots k$, $\cdots p$. We need consider only those modalities in which the two stimuli are different.

We consider two mechanisms, either of which may be used. First, let us assume that there is a discriminatory center represented by the mechanism of Figure 1 (A) but in which the fibers *I* and *II* of the figure represent respectively a number of fibers from the sense organs of various modalities. Let these fibers be at least p-fold so that at synapse s_1 [Figure 1 (A)] there corresponds to each S_k a value $\varepsilon_k(S_k)$ for the excitation factor. The stimulus S then excites each of the fibers represented by *I* of Figure 1 (A) by the respective amounts $S_1 \cdots S_p$ and the stimulus $\bar{S}$ excites the fibers represented by *II* of Figure 1 (A) by amounts $\bar{S}_1 \cdots \bar{S}_p$. Corresponding to each value $\bar{S}_k$ there is a value $\varepsilon_k(\bar{S}_k)$ at synapse s_2, Figure 1 (A). If we define $\bar{x}$ by

$$\bar{x} = \sum_{k=1}^{p} \varepsilon_k(S_k) - \sum_{k=1}^{p} \varepsilon_k(\bar{S}_k) \ , \tag{25}$$

so that $\bar{x}$ is the difference between the total excitation factor at s_1 and the total at s_2 [Figure 1 (A)], then the equations (11) to (15) of B may be used if x of those equations is replaced by $\bar{x}$ of equation (25). Since some of the fibers of *I* and *II* may be inhibitory, certain $\varepsilon(S)$ should be replaced by $j(S)$ (where j is the inhibitory factor) or we may formally permit ε to be negative in equation (25) to avoid complicating the notation, although ε is essentially a positive quantity.

Instead of the above described mechanism we may consider one slightly different. We may assume that within each modality there is a mechanism like that of Figure 1 (A). Then let the efferent ends of each of these mechanisms lead to a similar central mechanism. Let the fibers corresponding to a response to S lead to one synapse, s_1, and those fibers corresponding to $\bar{S}$ lead to another synapse, s_2. Then at s_1 the total excitation factor is proportional to the sum of all $\varepsilon_k(S_k) - \varepsilon_k(\bar{S}_k)$ for which $S_k > \bar{S}_k$ while at s_2 the total excitation factor is proportional to the sum of all $\varepsilon_k(\bar{S}_k) - \varepsilon_k(S_k)$ *for which* $S_k < \bar{S}_k$. Hence the difference between the excitations at s_1 and s_2 is proportional to $\varepsilon_k(S_k) - \varepsilon_k(\bar{S}_k)$ summed over all k's and thus is proportional to $\bar{x}$ of equation (25).

The two mechanisms described give the same result. They would not necessarily do so if we allow for possible effects of the modalities upon one another. Such interplay is quite likely to occur. For the time we shall consider only the simpler situations described above.

Since the modalities are not the same, the $\varepsilon(S)$ functions will vary with the modality, and hence the expressions $\varepsilon_k(S_k)$. These functions will increase monotonically with the S_k, each S_k being above some threshold value. Let us neglect the threshold values or assume that they are nearly equal. The graphs of the functions then begin near the origin and for at least a small range increase linearly. Over this range $\varepsilon_k(S_k)$ is proportional to S_k or, say, equal to $L_k\ \varepsilon(S_k)$, where ε is independent of the modality and any constants are absorbed in L_k. On the other hand, if each function $\varepsilon_k(S_k)$ may be approximated by a logarithmic relation over a rather wide range, or

$$\varepsilon_k(S_k) = L_k \log \frac{S_k}{h_k} ,$$

then, for approximately equal thresholds, we have $\varepsilon_k(S_k)$ proportional to $\log(S_k/h) = \varepsilon(S_k)$, and ε is again independent of k except through S. In either case and under even more general conditions, we may introduce the relation

$$\varepsilon_k(S_k) = L_k\varepsilon(S_k). \tag{26}$$

However, if the desired ranges in the S's are not near the origins and some relations are linear and some logarithmic, etc., an expression similar to (41), but with a constant term added, would be a fair approximation, or

$$\varepsilon_k(S_k) = L_k\ \varepsilon(S_k) + \varepsilon_{0k} . \tag{27}$$

Introducing either equation (26) or (27) into (25) we have

$$\bar{x} = \sum_{k=1}^{p} L_k\ \varepsilon(S_k) - \sum_{k=1}^{p} L_k\ \varepsilon(\bar{S}_k) \tag{28}$$

or

$$\bar{x} = \sum_{k=1}^{p} L_k\ x_k , \tag{29}$$

where

$$x_k = \varepsilon(S_k) - \varepsilon(\bar{S}_k) . \tag{30}$$

If we assume that the $\varepsilon(S)$ function is the same from individual to individual so that any constant factors are absorbed in the L's then $\varepsilon(S_k)$, and hence x_k, is a function of the stimulus only. The L's vary from individual to individual and are the weights which each individual accords to each modality. For example if two colored figures are being compared and it happens that one figure is accepted as being superior in form and the other is accepted as superior in coloring, the probability that an individual chooses one in preference to the other depends also on the relative weightings he gives to form and color in making the choice.

Although the above results are sufficiently general to include complex stimuli, we have treated the stimuli as if they possessed only physical attributes which could be measured. Some of the attributes which determine any judgment may not be physical. They may be entirely subjective and due only to a former association with the stimulus or a similar stimulus. Hence, some of the fibers leading to the center of discrimination arise directly from centers which have been conditioned to the stimuli in different degrees. If we give the proper set the subject may be able to inhibit all tendencies to respond on the basis of the physical attributes so that (since we neglect non-influencing factors) all the factors, p, [equation (29)] depend almost entirely upon the individual's past experience. An illustration would be the ranking of nationality preferences by patriots of the various nations.

Equation (29) has the form of the basic assumption in factor analysis (Thurstone, 1936) as the value $\bar{x}$ is proportional to the scale value of a certain comparison for a particular individual. If there are Q stimuli which are compared in all possible pairs (Guilford, 1936) there result $Q(Q-1)/2 = N$ test situations. Let these N test situations be presented to each of n individuals. By the scaling procedure (Guilford, 1936) we may obtain the value $\bar{x}_{ji}$ for individual i on test situation j. We then have the nN equations represented by

$$\bar{x}_{ji} = \sum_{k=1}^{p} x_{jk} L_{ki} \, . \tag{31}$$

If the stimuli are chosen so as not to be dissimilar in too many respects, then, for any pair of stimuli, only a few of the scale values, x_{jk}, will be appreciably different from zero. Under these conditions we would be justified in applying the factor analysis methods developed by L. L. Thurstone (1936). As it is only the correlations between the tests that are used in the analysis, one might substitute a very rough scale based on a simpler scaling method.

In some cases the scale values of equation (29) may be determined directly and, if so, would constitute a check on the factor procedure and on the assumptions made. By modifying the factor procedure so that covariances are initially used, the actual magnitudes of the L's and ε's could perhaps be derived in some common units. The process of correlating the results with information obtainable by other means should be simplified. It would also be of interest to notice the form of the distribution of the L's. By careful selection of the items it might be possible to eliminate negative L's — a negative L meaning an "unpleasant" attribute, being more strictly due to an inhibitory process or "negative ε".

It should be kept in mind that equation (29) would in general be an approximation to equation (25) and that certain simplifying assumptions have been made. In particular it may be noted that no possibility of intercorrelations among the k's is allowed since in the group of fibers I and II [Figure 1 (A)] no interplay was considered. In general, one would rather expect some slight interrelation to be present in any single individual. But unless such an effect were fairly uniform throughout the population it would not show up, but would contribute to the error space. The procedure suggested by equation (29) has been used as an empirical approach to the problem. The suggestion of the preceding paragraph may be of use in such an approach.

Summary. By applying the theory to the comparison of complex stimuli, more general results are obtained. Under certain assumptions the results directly indicate the method of factor analysis.

III. Applications to a multidimensional psychophysics. We have been considering discrimination between two stimuli which differed in more than one respect. From the very nature of the case we did not consider the possibility of the judgment being made from different points of view at different times. We might have assumed the more general situation in which each modality inhibited (or excited) every other, either as a function of the sum of the two components $S_k + \bar{S}_k$ or as a function of the difference, $S_k - \bar{S}_k$, or both. In this case, if either one modality was fairly prominent or if its difference was large, then the difference in magnitude in that modality might be the only factor affecting the judgment.

In the simpler case having no such interrelation, we always have a difference between two sums of excitation factors which determine the judgment. In this case it would not be possible to give a spatial representation to a set of deviates corresponding to various stimulus pairs, the deviates being proportional to the differences between sums of ε's. However, a spatial represention in this case can be obtained if we separate the components of such a deviate into a factor which is a function of the individual and another factor which is a function of the stimulus pair. But this returns to the method of factor analysis described in the preceding section. Even in the more complex case of interrelation between modalities there would not be a result representable by coordinates of ordinary space, though, approximately, some curved surface may be used for representation of the data.

A discussion of the possibility of representation of such data in spatial form has been given by Gale Young and A. S. Householder (1938). A rather elementary method for checking the possibility of spatial representation may be suggested here. Let stimuli be chosen varying in two modalities. Let them be chosen so that in many subgroups they vary in one modality only. If the stimuli are represented by S_{ij} then S_{i1}, S_{i2}, S_{i3}, etc., have equal magnitudes in modality i. With care in choosing the stimuli it would be possible to choose S_{1j}, S_{2j}, S_{3j}, etc., so that these had equal magnitudes in modality j. This is not necessary but simplifies the discussion. Since S_{i1}, S_{i2}, S_{i3}, etc., vary in one modality only, then from the judgments involving these stimuli the corresponding deviates are obtained. Let us assume that any adjustment necessary is made so that the distance S_{11} to S_{12} plus the distance S_{12} to S_{13} equals the distance S_{11} to S_{13}. Choosing S_{11} as the origin and any direction to represent variation of j, the points S_{11}, S_{12}, S_{13}, etc., are determined. Similarly S_{11}, S_{21}, S_{31}, etc., are determined along some other axis corresponding to i. But S_{21}, S_{22}, S_{23}, etc., can also be determined. Thus all points S_{ij} are determined (in fact highly over-determined). So far only variation of one modality at a time has been considered.

We may now determine the distances involving differences in both modalities as S_{11} to S_{22}, or S_{11} to S_{23}, etc. The simple case considered in the last section would require that the distance S_{11} to S_{22} would be equal to the sum of the distances S_{11} to S_{12} and S_{12} to S_{22}. If, however, a spatial representation is possible, then the square of the distance S_{11} to S_{22} will equal the square of the distance S_{11} to S_{12} plus the square of the distance S_{12} to S_{22} minus the product of these two distances times the cosine of the angle between the axes. For each composite distance we can determine a value for the angle which will satisfy that one set of data. Thus, there are a large number of ways of obtaining the angle. If these values of the angle are consistent, then we may represent the data on a plane. If, however, the value of the angle varies significantly depending on the distances chosen, a plane surface cannot be used though some curved surface may be satisfactory.

In order to obtain a psychological distance as discussed above, it is necessary that there be uncertainty in the judgments. The range over which there is a sufficient degree of uncertainty is generally very small compared with the entire range. The ratio of the two would be approximately the reciprocal of the number of just noticeable differences. In the above discussion of the possibility of a spatial representation of the data, we have been considering only a small range of the space at a time. If it is necessary to use a curved surface to represent a small range of values, it would be of little use to attempt a spatial representation of the entire range.

IV. Suggestions on the use of triads in psychophysics. The use of triads in presentation of stimuli for comparison judgments as suggested by M. W. Richardson (1938), has a number of advantages. However, in the manner of presentation used, a parameter is lost and hence certain information is lost. In making a judgment from a triad, one is essentially making a comparison among three stimuli. The latter may either be the three elements constituting the triad or the psychological distances between pairs, generally the latter. Now for such discrimination it was previously (A, p. 123) pointed out that one fraction of the correct judgments contain a false judgment. Hence, each of the respective proportions of judgments contain a certain fraction of false judgments and the situation is obscured.

Consider the case in which the elements of the triad are A, B, C. Let the judgments be made on the basis of similarity so that a is the number of judgments that B and C are most similar or B is "closest" to C., i.e. BC is the shortest psychological distance. Similarly let b be the number of judgments that, of the three elements, C and A are most closely related; and let c be the number of judgments that A and B are most closely related. We stated above that each of the number of judgments, as a, b, c, contain a fraction of false judgments. For instance, in deciding that AB is the shortest distance, a judgment contributing to the number c, the individual may have decided that BC was shorter than CA whereas the reverse may have been the case (as determined by the majority of individuals or by the majority of the same individual's judgments).

Now suppose that instead of permitting a choice from three responses, the triad is presented so that the choice is limited to one of two responses. A particular triad would then have to be presented three times, as, AB compared with BC, BC with CA, and CA with AB. Let the triad be presented in such pairs a number of times. For the first pair, the comparison of the psychological distance AB with BC, let γ_1 be the number of judgments $AB > BC$ and let α_1 be* the number of judgments $BC > AB$. Similarly let α_2 be the number of judgments of $BC > CA$, and let β_2 be the number of judgments $CA > BC$ in the second pair. Similarly for the third pair let β_3 and γ_3 be the numbers of judgments $CA > AB$ and $AB > CA$ respectively. Now it is the respective ratios which are constant, not the numbers, which naturally depend upon the number of presentations. Let us then multiply both numbers from the second pair, α_2 and β_2 by the fraction α_1/α_2 and define $\beta_1 = \beta_2\, \alpha_1/\alpha_2$. Then the numbers α_2 and β_2 may respectively be replaced by α_1 and β_1. Similarly let us multiply both numbers from the third pair, β_3 and γ_3 by the fraction β_1/β_3 and define

$$\gamma'_1 = \frac{\alpha_1}{\alpha_2}\frac{\beta_2}{\beta_3}\gamma_3 \,. \tag{32}$$

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* The α's in this section are not to be confused with the α's in section *I*. They denote different things.

Then the numbers β_3 and γ_3 may be replaced by the quantities β_1 and γ'_1. Now γ'_1 is a given number since α_1, α_2, β_2, β_3, and γ_3 are numbers experimentally obtained. The quantity γ_1 is similarly an experimental value. Hence in general $\gamma_1 \neq \gamma'_1$. There are then four independent values, as α_1, β_1, γ_1 and γ'_1. Other sets of four values are sufficient but there must be four. In the previously mentioned manner of presentation only three values would be obtained, a,b,c. Only if γ_1 should be equal to γ'_1 would it be possible to consider the similarity of the two sets of values.

We next investigate conditions under which we should expect γ'_1 of equation (32) to equal γ_1. For simplicity consider the differences AB, BC, and CA as being the stimuli being compared and let $AB > BC > CA$. Experimentally we obtain as above, γ_1, α_1, α_2, β_2, β_3 and γ_3. Then corresponding to the ratio $\gamma_1/(\gamma_1 + \alpha_1)$ we obtain the probability

$$P_{ABBC} = \frac{\gamma_1}{\gamma_1 + \alpha_1} \tag{33}$$

that AB is judged greater than BC. Let $X_{\gamma_1\alpha_1}$ be the deviate corresponding to P_{ABBC}. Then

$$\varepsilon_{\gamma_1\alpha_1} = \sigma_1 X_{\gamma_1\alpha_1}. \tag{34}$$

Similarly, from α_2 and β_2

$$P_{BCCA} = \frac{\alpha_2}{\alpha_2 + \beta_2} \tag{35}$$

and $X_{\alpha_2\beta_2}$ is the deviate corresponding to P_{BCCA}, then

$$\varepsilon_{\alpha_2\beta_2} = \sigma_2 X_{\alpha_2\beta_2}. \tag{36}$$

And from β_3 and γ_3

$$P_{CAAB} = \frac{\beta_3}{\beta_3 + \gamma_3}, \tag{37}$$

so that if $X_{\beta_3\gamma_3}$ is the deviate corresponding to P_{CAAB}, and $X_{\beta_3\gamma_3} < 0$, then

$$\varepsilon_{\beta_3\gamma_3} = \sigma_3 X_{\beta_3\gamma_3}. \tag{38}$$

As in equation (30) we may write

$$\begin{aligned} \varepsilon_{\gamma_1\alpha_1} &= \varepsilon_{AB} - \varepsilon_{BC}, \\ \varepsilon_{\alpha_2\beta_2} &= \varepsilon_{BC} - \varepsilon_{CA}, \\ \varepsilon_{\beta_3\gamma_3} &= \varepsilon_{CA} - \varepsilon_{AB}. \end{aligned} \tag{39}$$

The relations (39) hold provided we consider the simple case with no interrelation between the modalities, and if we assume no change in the parameters, in particular, no change in the relative weightings or "point of view". From (39) it is evident that

$$\varepsilon_{\gamma_1\alpha_1} + \varepsilon_{\alpha_2\beta_2} + \varepsilon_{\beta_3\gamma_3} = 0 \, . \tag{40}$$

Hence, if in addition to the requirements just mentioned, we add the condition that the standard deviations are unchanged, or if

$$\sigma_1 = \sigma_2 = \sigma_3 \tag{41}$$

then from (34), (36), (38) and (40)

$$X_{\gamma_1\alpha_1} + X_{\alpha_2\beta_2} + X_{\beta_3\gamma_3} = 0 \, . \tag{42}$$

But when this condition holds, then, unless at least two of the distances are equal, a very special case, it is impossible for γ_1 to equal γ'_1. That this is so can be verified by taking any numbers $\alpha > \beta > \gamma$ and obtaining the deviates from the proportions $\gamma/(\gamma + \alpha)$, $\alpha/(\alpha + \beta)$ and $\beta/(\beta + \gamma)$. The sum will not be zero whereas by (42) the sum of deviates is zero. Hence the data, if they are represented by the mechanism, cannot be represented by the three values alone. We may also conclude that the proportions obtained according to the first discussed method, from which only three values a, b, and c are obtained, cannot be used to determine corresponding deviates.

It should be pointed out that, since ε_{AB}, ε_{BC} and ε_{CA} must be nearly equal in a choice situation, if (40) and (41) hold, then (42) will be nearly correct. On the other hand, if (41) does not hold, or if there may have been some change in the parameters depending upon which "sides" of the triad are being judged, then (42) might not be even approximately true so that γ_1 would not even be approximately equal to γ'_1. Conversely, if γ'_1 differs widely from γ_1 in a case for which the distances AB, BC and CA are nearly equal, then the difference would be interpreted as due to a change in some parameters with a change in the pair of the triad to be judged. No attempt at this point will be made to give possible explanations on the basis of the mechanism of such a behaviour, should it occur.

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NERVE CONDUCTION THEORY: SOME MATHEMATICAL CONSEQUENCES OF BERNSTEIN'S MODEL

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The generally accepted permeability theory of nerve conduction is presented in mathematical form. The resulting velocity formula is found to agree well with data on squid giant axon, but predicts velocities considerably too high in the case of *Nitella*. The dependence of velocity on fiber diameter is discussed for both medullated and non-medullated nerve, it being shown theoretically that velocity is proportional to the square root of diameter for non-medullated and to the diameter for medullated nerve. The equations relating the shape of the action spike to the observed permeability changes are given but are not solved.

Conduction of the irritable response, while occurring in all types of living matter (Heilbrunn, 1938, chap. 38), has been most extensively studied, both theoretically and experimentally, in nerve. Three separate assumptions (verified in greater or lesser degree) have been fundamental in most discussion of the nerve conduction problem. These are:

1. The hypothesis of local re-excitation by action currents, first put forward explicitly in 1872 by L. Hermann (1899).
2. The hypothesis of the nerve as a resistance-capacitance network; that is, that a nerve may be considered, as far as electrotonus is concerned, as a cable-like, linear electrical network. This point of view is sometimes attributed to J. L. Hoorweg (Cremer, 1909).
3. The hypothesis of permeability change; that is, that excitation at a given point is characterized by an increase in membrane permeability at that point. This is the basis of the J. Bernstein (1912) theory and has been extended by R. Lillie (1923).

These three assumptions have come to be so widely accepted that diagrams of nerve conduction incorporating the first and third hypotheses are given in the standard elementary physiology texts (e.g. A. J. Carlson and V. Johnson, 1937), while the second hypothesis has been used in almost all of the more exact treatments of conduction phenomena. In the present paper we shall give a quantitative account of nerve conduction which embodies these three fundamental hypotheses; the related phenomena of excitation, and questions regarding the validity of these assumptions will not be considered here.

I. Historical. To place the present theory in its proper perspective we shall briefly recall some previous attempts to treat the problem of nerve conduction quantitatively. One of the first of the modern theories* was put forward by M. Cremer (1923), who obtained a formula for the velocity of propagation, but did not work out the details of the process. It appears that Cremer's results are included under a later more detailed theory of N. Rashevsky (1938). K. Umrath (1928), working with sensitive plants rather than nerves, appears to have given the first quantitative account of a feasible conduction theory involving a differential equation of propagation. His was a sort of "chemical fuse" theory, the excited region producing a substance which diffused ahead and ultimately brought about excitation at other points when its concentration there reached a certain critical value.

Rashevsky (1931, 1933, 1935, 1938) considered the spread of action currents in a pure resistance network, used a formal excitation theory to describe the establishment of excitation by these currents, and represented the occurrence of excitation by the sudden insertion of a battery in the circuit at the point in question. By using different excitation equations he obtained slightly different conduction theories. He also considered myelinated nerve fibers, with excitation occurring only at the Ranvier nodes and conduction taking place by the disturbance "jumping" from node to node. W. Rushton (1937) gave a similar treatment, except that instead of using a formal excitation equation he supposed excitation to occur when the membrane became sufficiently depolarized. His theory is equivalent to one of Rashevsky's (Weinberg, 1940).

A somewhat unsuccessful attempt to extend Rashevsky's theory by including the membrane capacitance as an element in the Hoorweg network has been made by A. M. Weinberg, (1939). The problem can, however, be effectively handled by the methods used in the present article.

The Rashevsky-Rushton theories introduce excitation formally as the sudden appearance of an E.M.F. in the circuit representing the nerve. In 1938 K. Cole and H. Curtis replaced this assumption by that of Bernstein; namely, that *the essential event which marks the occurrence of excitation is a decrease in the transverse resistance of the membrane.* In their paper, however, these authors were not primarily interested in giving a complete theory of conduction, and so they did not attempt to derive a velocity formula. In the present work* we shall extend Cole and Curtis's formulations with the purpose of obtaining a velocity formula and describing quantitatively as many details of the conduction process as possible.

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* We are disregarding earlier theories of L. Hermann (1899) and Broemser (1921, 1924) since they do not seem to conform to the modern point of view.

II. The Bernstein Model. Bernstein supposes the resting membrane to be polarized, i.e., to sustain a potential difference (corresponding to the resting or demarcation potential) like a charged condenser. If the two sides of the membrane condenser be connected by a conductor there will be a passage of current and the charge will decrease. If the conductor is removed the charge builds up to its original value, but this will not occur instantly. There is a time delay in the recharging process, as if the condenser is supplied from a battery through a series resistor. Specifically, Bernstein and Lillie picture the membrane as permeable to one ion of a solute but not to the other, so that a potential difference is set up at the membrane (Heilbrunn, p. 316; Erlanger and Gasser, p. 133). If the ions are removed from the surface it takes time for fresh ones to diffuse out from the interior, so that the resistance through which the battery supplies the condenser may be essentially a diffusion resistance. The membrane is not completely impermeable to the other ion, so that the condenser is shunted by a leak resistance. Excitation is accompanied by a decrease in this shunting resistance.

Picturing each infinitesimal element of the membrane in this way and linking the elements together by resistances corresponding to the longitudinal resistances of the interior and exterior regions of the nerve fiber, we have a network as shown in Figure 1a. Here r_i and r_e are respectively the internal and external resistances per unit length; C is the capacitance of the membrane per unit length; $1/\rho$ is the transverse conductance of the membrane per unit length; E is the voltage

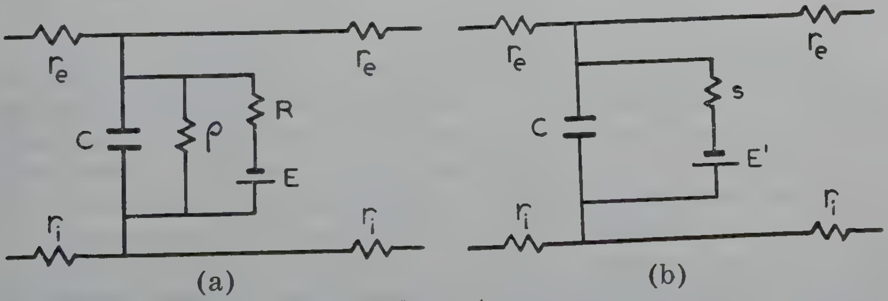

FIGURE 1.

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* The main results presented in this paper were obtained by F.O. in 1937 and reported in abstract form (Offner, 1939); they were arrived at independently by G.Y. and A.W. in 1939.

of the battery which charges the membrane; and $1/R$ is the internal conductance of the battery per unit length. The total conductance per unit length, $1/s$, between the interior and exterior of the nerve will be the sum of the membrane and battery conductances, and the sum of r_i and r_e will be denoted by M:

$$\begin{aligned} s &= R\,\rho/(R+\rho)\,, \\ M &= r_i + r_e\,. \end{aligned} \tag{1}$$

The network of Figure 1a is the same as one discussed by Gerard (1930, p. 521), which is very similar to the one suggested by Cole and Curtis (1938), shown in Figure 1b. They considered that the total transverse resistance may be identical with the internal resistance of the battery. The two networks are equivalent (for the conduction problem) if E' is equal to Es/R. The present picture however, accounts for the simultaneous change in both the measured membrane potential and permeability by assuming a change in the single parameter ρ; it is also slightly more general since it allows for a continual expenditure of energy (represented by the flow of current through R and ρ) to maintain a polarization of the membrane. This energy may be associated with a portion of the resting metabolic energy expenditure required to maintain the polarization. (Gerard, 1930).

By a standard application of circuit theory (Cole and Curtis, 1938) the differential equation satisfied by V, the potential difference between inside and outside of the core, is found to be

$$\frac{\partial^2 V}{\partial x^2} - \frac{M}{s} V - MC\frac{\partial V}{\partial t} = -\frac{M}{R} E\,, \tag{2}$$

where x denotes distance along the nerve and t is time.

According to the permeability hypothesis ρ, and therefore s, is supposed to decrease when excitation occurs.* Excitation will be assumed to take place when a given point is sufficiently depolarized; that is, when V at a point drops to some critical value V_c. When excitation does occur, the membrane thus "breaks down" in the sense that its transverse resistance drops to a fraction of its resting value. A little later the membrane returns to its original semipermeability, s returning to its former value; the nerve then returns ultimately (though somewhat later than s) to its original state. The intimate nature of the breakdown-recovery cycle undergone by the membrane is not completely understood; but we may very roughly approximate the cycle if we suppose s to drop suddenly to a smaller value s_0, remain there for a time τ of the order of the absolute refractory period, and then rise suddenly to its original value s. This simple case will serve as an illustration, and we turn now to its consideration.

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* More generally, all the quantities ρ, R, r_i, r_e, C, and E may change, but it is probably not too far wrong to think of them as all constant except ρ; Cole and Curtis (1939) find that C changes by not more than 2% during action in a giant axon of squid, and the change in M is probably very small also.

III. U-Shaped Conductance Wave. Consider a disturbance moving along a nerve with velocity v. An observer moving along with it would, on the supposition just made, see a contour for the total transverse resistance s as shown in Fig. 2. At the front end of the excited region the resistance drops from s to s_0 while at a distance $v\tau$ behind this point it regains its original value.* If the propagation has reached a steady state with constant velocity, the voltage contour V will also be fixed and unvarying to the observer; i.e., in (2) we have a solution in the form

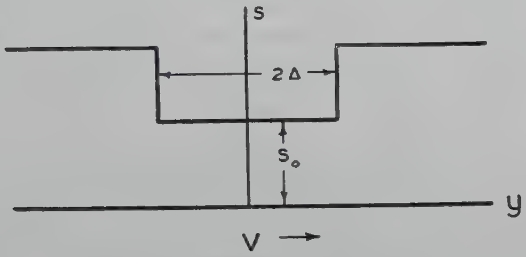

FIGURE 2.

$$V = V(x - vt), \tag{3}$$

$y = x - vt$ being the distance measured along the nerve from a point moving with the disturbance.** As depicted in Fig. 2, the disturbance partitions the nerve into three sections in each of which, under our present assumptions, (2) applies with constant coefficients. Equations (2) and (3) give for V as a function of y,

$$\frac{d^2V}{dy^2} + vMC\frac{dV}{dy} - \frac{M}{s}V = -\frac{M}{R}E, \tag{4}$$

---

* The experimental curve giving the time variation of s during activity (Cole and Curtis, 1939) suggests that a better approximation to the actual s contour would be obtained if s_0 is assumed to return to some value s_1, $s_0 < s_1 < s$, instead of to its original value after the time τ. The details of the analysis are essentially the same as in the present case and so will be omitted for simplicity.

** Umrath employed this same steady state solution while Rashevsky used an integral formulation and did not assume in advance that the velocity was constant.

which is the space differential equation for the steady V contour moving with the disturbance in steady state conduction. The general solution of (4) is

$$V = \frac{s}{R} E + Ae^{\alpha y} + Be^{\beta y} \, , \tag{5}$$

where $\omega = \alpha$ and $\omega = \beta$ are roots (assumed distinct) of the quadratic equation

$$\omega^2 + vMC\omega - M/s = 0 \tag{6}$$

and A and B are integration constants. It may be noted here that α and β have opposite signs; for definiteness, we suppose $\beta > 0$, $\alpha < 0$.

Denoting the length of the depression in the s contour by $2\,\Delta$ and taking the origin for y at the center of this region, we have

$$\begin{aligned} V_1 &= E' + A_1 \, e^{\alpha y} + B_1 \, e^{\beta y} && (y > \Delta) \\ V_2 &= E'_0 + A_2 \, e^{\alpha_0 y} + B_2 \, e^{\beta_0 y} && (-\Delta < y < \Delta) \\ V_3 &= E' + A_3 \, e^{\alpha y} + B_3 \, e^{\beta y} && (y < -\Delta) \end{aligned} \tag{7}$$

where $E' = Es/R$ is the resting voltage at a point far ahead of the excited region and the zero subscript on a quantity denotes that s has been replaced by s_0 in the original quantity. E'_0 is the voltage which would exist in the excited region far from the junction, if the breakdown persisted indefinitely.

To evaluate the integration constants, the following boundary conditions are used:

a) V is finite at $y = \pm \infty$.

b) By Kirchhoff's laws, the voltage and current, and therefore V and dV/dy , are continuous at the junction points $y = \pm \Delta$.

From the first boundary condition, it follows immediately that $B_1 = A_3 = 0$, while the other boundary conditions will be satisfied if

$$\begin{aligned} A_1 &= (E' - E'_0) J_1/D \\ A_2 &= (E' - E'_0) J_2/D \\ B_2 &= (E' - E'_0) J_3/D \\ B_3 &= (E' - E'_0) J_4/D \end{aligned} \tag{8}$$

where

$$\begin{aligned} J_1 = \beta(\alpha_0 - \beta_0) \, e^{(2\alpha_0 - \alpha)\Delta} &+ \beta_0(\beta - \alpha_0) \, e^{-\alpha\Delta} \\ &- \alpha_0(\beta - \beta_0) \, e^{(2\alpha_0 - 2\beta_0 - \alpha)\Delta} \end{aligned}$$

$$J_2 = \beta(\alpha - \beta_0) \, e^{\alpha_0\Delta} - \alpha(\beta - \beta_0) \, e^{(\alpha_0 - 2\beta_0)\Delta}$$

$$J_3 = \alpha(\beta - \alpha_0)\, e^{-\beta_0\Delta} - \beta(\alpha - \alpha_0)\, e^{(2\alpha_0-\beta_0)\Delta} \tag{9}$$

$$\begin{aligned} J_4 = {} & \alpha(\beta_0 - \alpha_0)\, e^{(\beta-2\beta_0)\Delta} + \alpha_0(\alpha - \beta_0)\, e^{\beta\Delta} \\ & - \beta_0(\alpha - \alpha_0)\, e^{(2\alpha_0-2\beta_0+\beta)\Delta} \end{aligned}$$

$$D = (\alpha - \beta_0)(\beta - \alpha_0) - (\alpha - \alpha_0)(\beta - \beta_0)\, e^{2(\alpha_0-\beta_0)\Delta} .$$

From (7), (8) and (9), the voltage at the front junction, V_c, is

$$V_c = E' + (E' - E'_0) \times \frac{\beta(\alpha_0 - \beta_0)\, e^{2\alpha_0\Delta} + \beta_0(\beta - \alpha_0) - \alpha_0(\beta - \beta_0)\, e^{2(\alpha_0-\beta_0)\Delta}}{(\alpha - \beta_0)(\beta - \alpha_0) - (\alpha - \alpha_0)(\beta - \beta_0)\, e^{2(\alpha_0-\beta_0)\Delta}} , \tag{10}$$

which for Δ large tends to

$$V_c = E' - \frac{\beta_0}{\beta_0 - \alpha}(E' - E'_0) . \tag{11}$$

It may be noted that the quantity V_c is simply the voltage at the front junction between excited and unexcited regions. Bernstein supposed the membrane to break down when it had been sufficiently depolarized — that is when V had reached some critical value V'_c. If the breakdown is instantaneous, then V_c and V'_c are identical; but, if as is probably the case, there is a time delay between excitation (or attainment of the critical voltage), and the breakdown of the membrane, then V_c and V'_c will be different. In the present theory only V_c, which can be determined directly from the point of inflection of the action spike is used, and *so the calculation of the velocity is independent of the excitation criterion used.* In the discussion of the dependence of velocity on diameter the further assumption is made that V_c (or more accurately E'/V_c) for a given kind of nerve is independent of the diameter.

The voltage at the point $y = -\Delta$ where the membrane resistance suddenly returns to its original value is given by an analagous expression which for Δ large tends to

$$V_h = E' + \frac{\alpha_0}{\beta_0 - \alpha}(E' - E'_0) . \tag{12}$$

The roots of (6) are of the form

$$\begin{aligned} \beta &= b - a \\ \alpha &= -b - a \end{aligned} \tag{13}$$

where $b > a > 0$, $a = a_0$ and $b_0 > b$. In terms of these quantities (11) and (12) become

$$V_c = E' - \frac{b_0 - a}{b_0 + b}(E' - E'_0) \tag{14}$$

and

$$V_h = E' - \frac{b_0 + a}{b_0 + b}(E' - E'_0) \; . \tag{15}$$

Thus it is seen that, at least for Δ large, the voltage wave is not symmetrical about the line $y = 0$; V is greater at the moment the membrane breaks down than at the moment it regains its original semipermeability.

IV. Velocity of Impulse. We have in equation (10) a relation from which to determine the steady state conduction velocity in terms of the nerve parameters. However, if we use the data on squid axon or *Nitella,* we find that if the excited region exceeds 0.6 cm., equation (11) is a very close approximation to the more exact equation (10), the error involved in neither case exceeding 1 part in 500. Since the measured crest time for 12 meter per sec. conduction is about 5×10^{-4} sec., the excited region is certainly larger than 0.6 cm., and we may safely use equation (11) ; in other words, we may neglect the effect upon points ahead of the advancing wave due to the recovery of the membrane in its wake. This was done by Rashevsky and Rushton who simply considered the disturbance as leaving the nerve permanently altered behind it. This simplification tends to very slightly (less than 0.1%) overestimate the conduction velocity.

From (14) we find

$$\frac{b_0 - a}{b_0 + b} = K \tag{16}$$

where

$$K = (E' - V_c)/(E' - E'_0) \; . \tag{17}$$

From (13) and (6) it is seen that

$$\begin{aligned} 2a &= vMC \, , \\ b &= \sqrt{a^2 + 1/L^2} \, , \\ \frac{1}{L^2} &= M/s \; . \end{aligned} \tag{18}$$

After some algebraic operations involving repeated squarings, (16) gives

$$4\,Ka^2 = \frac{[K/L^2 - (1-K)^2/L_0^2]^2}{(K-K^2)/L^2 + (1-K)^2/L_0^2} \; ; \tag{19}$$

or, from (18)

$$v = \frac{\lambda_0^2\, s - \lambda^2\, s_0}{C\sqrt{M\,\lambda\,\lambda_0\, s s_0 (\lambda + \lambda_0)(\lambda\, s + \lambda_0\, s_0)}}\,, \tag{20}$$

where $\lambda = (E'/V_c) - 1$, $\lambda_0 = 1 - (E'_0/V_c)$.* If $s_0 << s$, and λ and λ_0 are of the same order of magnitude, we may neglect $\lambda^2\, s_0$ compared with $\lambda_0^2 s$, and $\lambda_0 s_0$ compared with λs. Formula (20) then becomes

$$v = \frac{\lambda_0^2}{C\lambda\sqrt{M s_0\, \lambda_0 (\lambda + \lambda_0)}} \tag{21}$$

while if $E'_0 << V_c$ so that $\lambda_0 \infty 1$,

$$v = \frac{1}{C\,\lambda\sqrt{M s_0 (1 + \lambda)}}\,. \tag{22}$$

Equation (22) for the velocity may be compared with some experimental data on squid giant axon given by Cole and Curtis (1939) and Cole and Hodgkin (1939). For an axon of diameter $d = 500\mu$, the following data are given:

Capacity $= 1 \times 10^{-6}\ fd/\mathrm{cm}^2$ so that $C = \pi\, d \times 10^{-6}$
$= 1.5 \times 10^{-7}\ fd/\mathrm{cm}$.
Membrane resistance during activity = 25 ohms
cm² so that $s_0 = 25/\pi d = 160$ ohms cm.
Specific resistance of sap = 34 ohms cm so that r_i
$= 136/\pi\, d^2 = 1.7 \times 10^4$ ohms/cm.

External resistance in oil $= 6.2 \times 10^4$ ohms/cm. According to Cole and Hodgkin's measurements, in sea water the characteristic length, $L\,(L^2 = s/M)$ is 2.6 times the characteristic length in oil. A simple calculation on the assumption that only the external resistance is changed when the axon is immersed in sea water shows that r_e in sea water is negligible compared to r_i so that

$$M = r_i = 1.7 \times 10^4 \text{ ohms/cm}.$$

The constant λ can be approximated from the inflection point of the rising action potential spike. The permeability change occurs at the time when the action spike is inflected; the voltage at this point

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* The steps leading to (20) are essentially the same if C is also allowed to change, say to C_0; the result in this case turns out to be

$$v = \frac{\lambda_0^2\, s - \lambda^2\, s_0}{\sqrt{M s s_0\, \lambda\, \lambda_0\, C C_0 (\lambda + \nu\, \lambda_0)(\lambda_0\, s_0\, \nu^3 + \lambda s)}} \tag{20 A}$$

where $\nu = C_0/C$. If $C = C_0$, $\nu = 1$, and (20 A) reduces to (20).

may be taken as V_c. (A slight correction [which is negligible if s_0 is sufficiently small] might be made since the recorded action spike maximum differs from the negative of V by a quantity of the order of E'_0). Using the squid action trace roughly corrected for amplifier response and electrode width (Cole and Curtis, 1939), λ may be estimated to be about 1.1. With this value of λ, equation (22) gives $v = 25$ meters/second, a value which agrees, within limits of experimental error, with Hodgkin's (1939) value for velocity of conduction in squid axon immersed in sea water.

In *Nitella,* the present theory predicts conduction velocities about 100 times too high. This may be due to structural complications neglected herein (double membrane) as well as the relatively slow conduction change.

The effect on the velocity of immersion in oil can be calculated if the assumption is made that only M changes when the external medium is changed. For squid axon in oil $M = 7.8 \times 10^4$ ohms/cm, while in sea water, $M = 1.7 \times 10^4$ ohms/cm. The ratio between the two M values is 4.5 so that from (22), the velocities should be in the ratio 1 to $\sqrt{4.5}$; this is approximately the ratio found by Hodgkin for squid axon immersed in sea water and in air or oil.

Equations (20-22) express the velocity of conduction as a function of the electrical constants of the nerve. To determine how v varies with d, the axon diameter, certain assumptions must be made concerning the variation of the electrical parameters with d. The most plausible assumptions seem to be the following:

a) The electrical parameters (membrane capacity, resistivity and membrane conductivity), when reduced to absolute units (e.g., membrane capacity per sq. cm.) are independent of the diameter.

b) λ and λ_0, being dimensionless, are independent of d. From assumption (a) it follows that the electrical parameters which are measured *per unit length of axon,* vary thus:*

$$r_i \propto 1/d^2, \qquad s, s_0, C \text{ all } \propto d.$$

For an axon in sea water (and probably in vivo), $r_e << r_i$ so that $M \infty r_i \propto 1/d^2$.

Using these assumptions in equation (20), we find

$$v = k\, d^{\frac{1}{2}} \tag{23}$$

where k is a proportionality constant. The only data on non-myelinated fibers (Pumphrey and Young, 1939) indicates approximately such a dependence of velocity on diameter ($v = kd^n$ where $n = 0.614 \pm .021$).

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* The assumption that $r_i \propto 1/d^2$ is not accurate if the axon is so large that the action current density is not spread uniformly over a cross section.

The present model, although closest to a non-myelinated axon, may be applied to a medullated axon if the fundamental assumptions are made that action occurs only at the Ranvier nodes but that the nodes are so close together that a continuous network may be used to approximate the discontinuous one assumed to represent the actual nerve (Weinberg, 1939). From this point of view the resistance of the myelin is seen to be of no significance as long as it is very large; the myelin simply makes a discontinuous network out of a continuous one. The further assumptions are made:

a) The capacitance of the myelin sheath is negligible compared with that of the membrane. This is probably not too far wrong in view of the relative thickness of the sheath compared with the membrane.

b) The width of the Ranvier nodes is some function of d, say $F(d)$, and the internodal lengths are some other function $f(d)$.

c) As in the non-myelinated case, the electrical parameters measured per unit dimension are independent of the diameter.

Under these assumptions we find

$$C, s \propto d \times F(d)/f(d)\,;\ M \propto 1/d^2$$

so that

$$v = k\sqrt{\frac{f^3(d)}{F^3(d)^d}} \tag{24}$$

There is some evidence to show that $f(d) = k'd^m$, where $m \infty 1$ (Gerard, 1931); unfortunately, as far as we know, no measurements to determine $F(d)$ have been made. If we make the simplest assumption, namely $F(d) =$ constant, then we find

$$v = kd\,. \tag{25}$$

Evidence on the relation between conduction velocity and fiber diameter for myelinated nerve is conflicting. It is generally agreed, however, that $v \propto d^m$ but values of m range from 1 to 2 (Erlanger and Gasser, 1937). The most recent work (Hursch, 1939) supports $v = kd$.

It is unfortunate that in none of the experimental work have $f(d)$ and $F(d)$ been determined together with v — and it is clear that internodal length and width of the Ranvier nodes, as well as diameter explicitly, determine the explicit functional relation between velocity and diameter according to the present theory. Since the form of $f(d)$ and $F(d)$ may vary considerably from fiber to fiber, the possibility exists that those authors who report $m > 1$ are working in a range where internodal length and diameter are not strictly proportional, or nodal width is not independent of the diameter.

The predictions of the present theory on variation of velocity with diameter are not peculiar to this particular theory. For example, the Rashevsky-Rushton velocity formula*

$$v = \frac{L\,\sigma}{C\,s}\,, \tag{26}$$

where σ is the dimensionless safety factor (Gerard, 1932; Tasaki, 1939; Rushton, 1937) and L is the characteristic length, leads to the same general dependence on diameter as the present theory. In fact, probably any linear network theory of this type will lead to a similar $v(d)$ function.

V. The Membrane Cycle. The model discussed in this paper can be generalized if, in the original equation (4), the coefficients are any assigned functions of y, depending on how the circuit constants at a point of the nerve fiber change as an impulse passes by. Presumably one would have to resort to numerical integration or to the use of machines such as the M.I.T. integraph in this case, since analytical solution of (4) with coefficients arbitrary functions of y is not generally possible. Sufficient data for such a calculation are afforded by the work of Cole and his associates, but the labor involved is considerable unless a machine is used.

However, we may invert the point of view and use the shape of the observed voltage contour or action spike to tell us something about the variation of the coefficients in (4). If we suppose only s to vary we can, assuming that the constant values of the remaining coefficients are known, determine s as a function of y by rewriting (4) as

$$\frac{1}{s} = \frac{1}{M}\frac{V''}{V} + vC\frac{V'}{V} + \frac{E}{R}\frac{1}{V}\,, \tag{27}$$

where primes denote derivations with respect to y.
From (29) we can calculate how s must vary in order to account for the observed action wave. Since derivatives of V are involved in (27),

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* If our formula (22), which is simplified from the more complicated (20), is written in terms of the characteristic length,

$$v = \frac{L_0}{C\,s_0\,\lambda\sqrt{1+\lambda}}\,, \tag{22A}$$

and the two formulae are seen to be similar in structure, although the excited region constants appear in (22A). If (20) were used, the constants of both regions would appear.

this method requires rather accurate determination of the observed wave form; it is, so to speak, rather sensitive to variations in wave shape. The derivatives of V have been determined experimentally by K. Cole and H. Curtis (1939) and by B. Katz and O. Schmitt (1940).

It can be readily seen from (27) that a symmetris s contour will not produce a symmetric V contour, for if V is symmetric the term in V is anti-symmetric while the remaining terms on the right are symmetric, so that $1/s$ is not symmetric. To produce a symmetric V wave, the value of $1/s$ would have to be greater on the leading side of the wave than at corresponding points on the trailing side.

In comparing (27) with experiment, it must be remembered that the recorded action spike, V_{act}, is related to V by

$$V_{act} = V_0 - V \tag{28}$$

where V_0 is a constant, at least if monophasic potentials are recorded with one electrode on a distant portion of the nerve. Substituting this value into (27)

$$\frac{1}{s} = \frac{1}{V_0 - V_{act}} \left(-\frac{V''_{act}}{M} - vC\,V'_{act} + \frac{E}{R}\right) . \tag{29}$$

Putting $E/R = \gamma$, we have

$$\frac{1}{s} = \frac{1}{V_0 - V_{act}} \left(-\frac{V''_{act}}{M} - vC\,V'_{act} + \gamma\right) , \tag{30}$$

so that, aside from a scale factor, $1/s$ depends on the two parameters γ and V_0. The other constants can be determined directly by experiment. In the case of *Nitella*, $v \propto 1$ cm/sec so that $vC << 1/M$ and (30) reduces to

$$\frac{1}{s} = \frac{1}{V_0 - V_{act}} \left(\gamma - \frac{V''_{act}}{M}\right) . \tag{31}$$

As was pointed out by Cole and Curtis, the theoretical $1/s$ and V curves should rise more steeply than the experimental curves because of the finite width of the recording electrodes. The exact correction due to the finite electrode width is difficult to calculate, although an experimental determination of its order of magnitude has been made by these authors. Since $1/s$ is very sensitive to small changes in V, an adequate comparison between theory and experiment is precluded until accurate, corrected values of V and its derivatives are available.

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